## (m) (m) 12. (m) (m) (m) (m) (m) Lan (L) 20. 14 19 14.1

- 1 CCCACGCGTC CGCATAAATC AGCACGCGGC CGGAGAACCC CGCAATCTCT GCGCCCACAA AATACACCGA CGATGCCCGA TCTACTTTAA GGGCTGAAAC GGGTGCGCAG GCGTATTTAG TCGTGCGCCC GCCTCTTGGG GCGTTAAGAGA CGCGGGTGTT TTATGTGGCT GCTACGGGCT AGATGAAATT CCCGACTTTG
- gGlyGlnAsn AlaProAlaA laSerGlyAl aArgLysArg HisGlyProGly 101 CCACGGGCCT GAGAGACTAT AAGAGGGTTC CCTACCGCCA TGGAACAACG GGGACAGAAC GCCCCGGCCG CTTCGGGGGC CCGGAAAAGG CACGGCCCAA GGTGCCCGGA CTCTCTGATA TTCTCGCAAG GGATGGCGGT ACCTTGTTGC CCCTGTCTTG CGGGCCGGC GAAGCCCCCG GGCCTTTTCC GTGCCGGGTC etG]\u00e4G]nAr
- uAlaArgGly AlaArgProG lyLeuArgVa lProLysThr LeuValLeuV alValAlaAl aValLeuLeu LeuValSerA laGluSerAla 201 GACCCAGGGA GGCGGGGGA GCCAGGCCTG GGCTCCGGGT CCCCAAGACC CTTGTGCTCG TTGTCGCCGC GGTCCTGCTG TTGGTCTCAG CTGAGTCTGC CTGGGTCCCT CCGCGCCCCT CGGTCCGGAC CCGAGGCCCA GGGGTTCTGG GAACACGAGC AACAGCGGCG CCAGGACGAC AACCAGAGTC GACTCAGACG ProArgGl 22
- LeulleThr GlnGlnAspL euAlaProGl nGlnArgAla AlaProGlnG lnLysArgSe rSerProSer GluGlyLeuC ysProProGl yHisHisIle GITGITCIGG ATCGAGGGT CGTCTCTCGC CGGGTGTTG TTTTCTCCAG GTCGGGGAGT CTCCCTAACA CAGGTGGACC TGTGGTATAG CAACAAGACC TAGCTCCCCA GCAGAGAGGG GCCCCACAAC AAAAGAGGTC CAGCCCCTCA GAGGGATTGT GTCCACCTGG ACACCATATC AGACTAGTGG 301 TCTGATCACC
- SerGluAspG lyArgAspCy sIleSerCys LysTyrGlyG lnAspTyrSe rThrHisTrp AsnAspLeuL euPheCysLe uArgCysThr ArgCysAspSer AGTOTTOTGO CATOTOTAAO GTAGAGGACG TTTATACOTG TOCTGATATO GTGAGTGACC TTACTGGAGG AAAAGACGAA CGCGACGTGG TCCACACTAA 401 TCAGAAGACG GTAGAGATTG CATCTCCTGC AAATATGGAC AGGACTATAG CACTCACTGG AATGACCTCC TTTTCTGCTT GCGCTGCACC AGGTGTGATT
- ProCysThrT hrThrArgAs nThrValCys GlnCysGluG luGlyThrPh eArgGluGlu AspSerProG luMetCysArg 501 CAGGTGAAGT GGAGCTAAGT CCCTGCACCA CGACCAGAAA CACAGTGTGT CAGTGCGAAG AAGGCACCTT CCGGGAAGAA GATTCTCCTG AGATGTGCCG CCTCGATTCA GGGACGTGGT GCTGGTCTTT GTGTCACACA GTCACGCTTC TTCCGTGGAA GGCCCTTCTT CTAAGAGGAC TCTACACGGC 1GluLeuSer GlyGluVa GTCCACTTCA 122
- 601 GAAGTGCCGC ACAGGGTGTC CCAGAGGGTT GGTCAAGGTC GGTGATTGTA CACCCTGGAG TGACATCGAA TGTGTCCACA AAGAATCAGG CATCATCATA CTTCACGGCG TGTCCCCACAG GGTCTCCCTA CCAGTTCCAG CCAGTAACAT GTGGGACCTC ACTGTAGCTT ACACAGGTGT TTCTTAGTCC GTAGTAGTAT LysCysArg ThrGlyCysP roArgGlyMe tValLysVal GlyAspCysT hrProTrpSe rAspIleGlu CysValHisL ysGluSerGl yIleIleIle

155

- GGAGTCACAG TTGCAGCCGT AGTCTTGATT GTGGCTGTGT TTGTTTGCAA GTCTTTACTG TGGAAGAAA TCCTTCCTTA CCTGAAAGGC ATCTGCTCAG CCTCAGTGTC AACGTCGGCA TCAGAACTAA CACCGACACA AACAAACGTT CAGAAATGAC ACCTTCTTTC AGGAAGGAAT GGACTTTCCG TAGACGAGTC 701
  - GlyValThrV alAlaAlaVa lValLeuIle ValAlaValP heValCysLy sSerLeuLeu TrpLysLysV alLeuProTy rLeuLysGly IleCysSerGly

## 

- GlyGlyGl yAspProGlu ArgValAspA rgSerSerGl nArgP‡oGly AlaGluAspA snValLeuAs nGluIleVal SerIleLeuG lnProThrGln CACCACCACC CCTGGGACTC GCACACCTGT CTTCGAGTGT TGCTGGACCC CGACTCCTGT TACAGGAGTT ACTCTAGCAC TCATAGAACG TCGGGTGGGT 801 GTGGTGGTGG GGACCCTGAG CGTGTGGACA GAAGCTCACA ACGAC¢TGGG GCTGAGGACA ATGTCCTCAA TGAGATCGTG AGTATCTTGC AGCCCACCCA 222
- GGTCCCTGAG CAGGAAATGG AAGTCCAGGA GCCAGCAGAG CCAACAGGTG TCAACATGTT GTCCCCGGG GAGTCAGAGC ATCTGCTGGA ACCGGCAGAA CCAGGGACTC GTCCTTTACC TTCAGGTCCT CGGTCGTCTC GGTTGTCCAC AGTTGTACAA CAGGGGCCC CTCAGTCTCG TAGACGACCT TGGCCGTCTT ValProGlu GlnGluMetG luValGlnGl uProAlaGlu ProThrGlyV alAsnMetLe uSerProGly GluSerGluH isLeuLeuGl uProAlaGlu 901 255
- 288 AlaGluArgS erGlnArgAr gArgLeuLeu ValProAlaA snGluGlyAs pProThrGlu ThrLeuArgG lnCysPheAs pAspPheAla AspLeuValPro CGACTITICCA GAGTUTUCTU CIUUGAUGAU CAAGGIUGIT IAUTHUCAUT AGGIGAUTU IGAGAUTUIG IUAUGAAGUI AUTGAAAUGI UIGAAUCAUG 1001 GCTGAAAGGT CTCAGAGGAG GAGGCTGCTG GTTCCAGCAA ATGAAGGTGA TCCCACTGAG ACTCTGAGAC AGTGCTTCGA TGACTTTGCA GACTTGGTGC
- PheAspSe rTrpGluPro LeuMetArgL ysLeuGlyLe uMetAspAsn GluIleLysV alAlaLysAl aGluAlaAla GlyHisArgA spThrLeuTyr 1101 CCTTTGACTC CTGGGAGCCG CTCATGAGGA AGTTGGGCCT CATGGACAAT GAGATAAAGG TGGCTAAAGC TGAGGCAGCG GGCCACAGGG ACACCTTGTA GGAAACTGAG GACCCTCGGC GAGTACTCCT TCAACCCGGA GTACCTGTTA CTCTATTTCC ACCGATTTCG ACTCCGTCGC CCGGTGTCCC TGTGGAACAT 322
- 1201 CACGATGCTG ATAAAGTGGG TCAACAAAAC CGGGCGAGAT GCCTCTGTCC ACACCCTGCT GGATGCCTTG GAGACGCTGG GAGAGAGACT TGCCAAGCAG IlelysTrpV alAsnLysTh rGlyArgAsp AlaserValH isThrLeuLe uAspAlaLeu GluThrLeuG lyGluArgLe uAlaLysGln GIGCTACGAC TAITITCACCC AGIIGITITIG GCCCGCICIA CGGAGACAGG IGIGGGACGA CCTACGGAAC CICIGCGACC CICICITGA ACGGIICGIC ThrMetLeu 355
- 1301 AAGATTGAGG ACCACTTGTT GAGCTCTGGA AAGTTCATGT ATCȚAGAAGG TAATGCAGAC TCTGCCWTGT CCTAAGTGTG ATTCTCTTCA GGAAGTGAGA TGGTGAACAA CTCGAGACCT TTCAAGTACA TAGATCTTCC ATTACGTCTG AGACGGAACA GGATTCACAC TAAGAGAAGT CCTTCACTCT uSerSerGly LysPheMetT yrLeuGluGl yAsnAlaAsp SerAlaXaaS erOC\* spHisLeuLe TTCTAACTCC LysileGluA
- GGAAGGGACC AAATGGAAAA AAGACCTTTT TCGGGTTGAC CTGAGGTCAG TCATCCTTTC ACGGTGTTAA CAGTGTACTG GCCATGACCT TCTTTGAGAG 1401 CCTTCCCTGG TITACCTITI TICTGGAAAA AGCCCAACTG GACTCCAGTC AGTAGGAAAG TGCCACAATT GTCACATGAC CGGTACTGGA AGAAACTCTC
- CCATCCAACA TCACCCAGTG GATGGAACAT CCTGTAACTT TTCACTGCAC TTGGCATTAT TTTTATAAGC TGAATGTGAT AATAAGGACA CTATGGAAAT GGTAGGTTGT AGTGGGTCAC CTACCTTGTA GGACATTGAA AAGTGACGTG AACCGTAATA AAAATATTCG ACTTACACTA TTATTCCTGT GATACCTTTA 1501

FIG.\_1B

1601 GICTGGATCA TICCGTITGT GCGTACTITG AGATTTGGTT TGGGAÜGTCA TTGTTTTCAC AGCACTTTTT TATCCTAATG TAAATGCTTT ATTTATTAT CAGACCTAGT AAGGCAAACA CGCATGAAAC TCTAAACCAA ACCCTACAGT AACAAAAGTG TCGTGAAAAA ATAGGATTAC ATTTACGAAA TAAATAAATA

1701 TTGGGCTACA TTGTAAGATC CATCTACAAA AAAAAAAAA AAAAAAAAG GGCGGCCGCG ACTCTAGAGT CGACCTGCAG AAGCTTGGCC GCCATGGCC AACCCGATGT AACATTCTAG GTAGATGTTT TTTTTTTTT TTTTTTTTC CCGCCGCGC TGAGATCTCA GCTGGACGTC TTCGAACCGG CGGTACCGG

LAPQQRAAPQQKRSSPSEGLCPPGHHISEDGRDCISCKYGQDYSTHWNDLLFCLRCTRCD KESGIIIGVTVAAVVLIVAVFVCKSLLWKKVLPYLKGICSGGGDPERVDRSSQRPGAED SGEVELSPÇTTTRNTVÇQÇEEGTFREEDSPEMÇRKÇRTGÇPRGMVKVGDÇTPWSDİEÇVH MEQRGQNAPAA|SGARKRHGPGPREARGARPGLRVPKTLVLVVAAVLLLVSAESALITQQD 121 61

**NVLNEIVSILQPTQVPEQEMEVQEPAEPTGVMLSPGESEHLLEPAEAERSQRRRLLVPA** 181 241

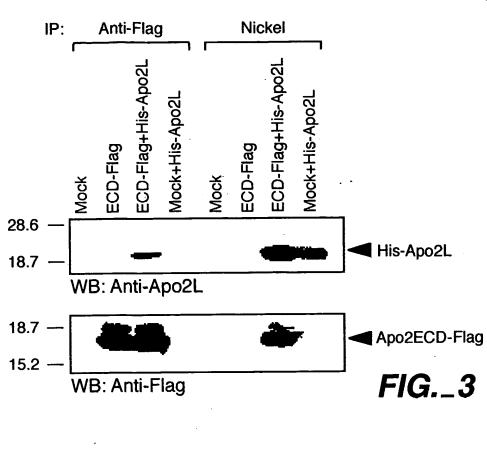
NEGDPTETLROCFDDFADLVPFDSWEPLMRKLGLMDNEIKVAKAEAAGHRDTLYTMLIKW VNKTGRDASVHTLLDALETLGERLAKQKIEDHLLSSGKFMYLEGNADSALS 301

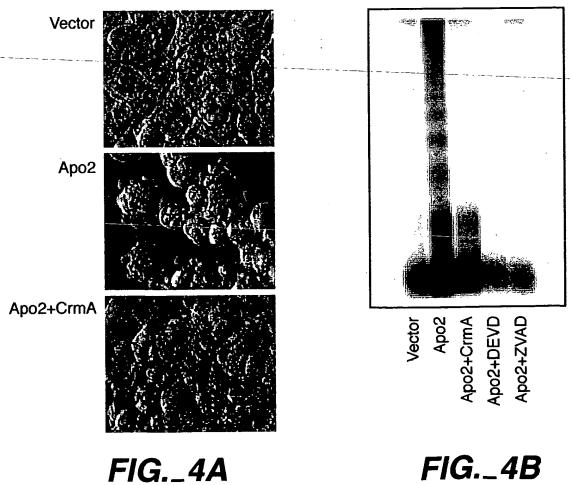
FADLVPFDSWEPLMRKLGLMDNEIKVAKAEAA - - GHRDTL FANIVPFDSWDQLMRQLDLTKNEIDVVRAGTA - - GPGDAL VMDAVPARRWKEFVRTLGLREAEIEAVEVEIGR - - FRDQQ VVENVPPLRWKEFVRLGLSDHEIDRIELQNGR - CLREAQ IAGVMTLSQVKGFVRKNGVNEAKIDEIKNDNVQDTAEQKV Apo3/DR3 Fas/Apo1 TNFR1 Apo2 DR4

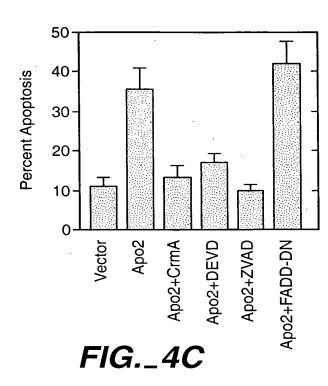
Apo3/DR3 TNFR1 Apo2 DR4

Fas/Apo1

YTMLIKWVNKTGRD - ASVHTLLDALETLGERLAKQKIED YEMLKRWRQQQP---AGLGAVYAALERMGLDGCVEDLRS YSMLATWRRRTPREATLELLGRVIRDMDLLGCLEDTEE -QLLRNWHQLHGKKEAY-DTLIKDLKKANLCTLAEKIQT YAMIMKWVNKTGRN-ASIHTLLDALERMEERHAKEKIQD







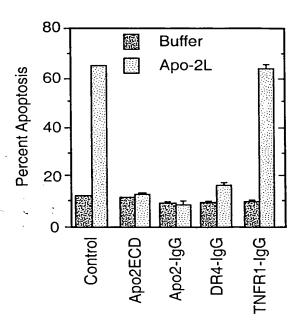


FIG.\_4D

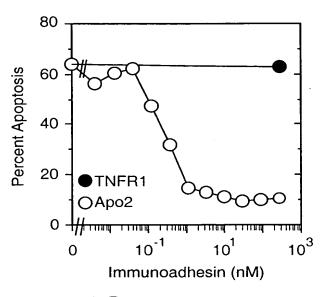


FIG.\_4E

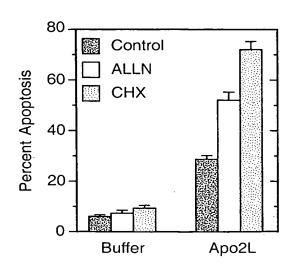
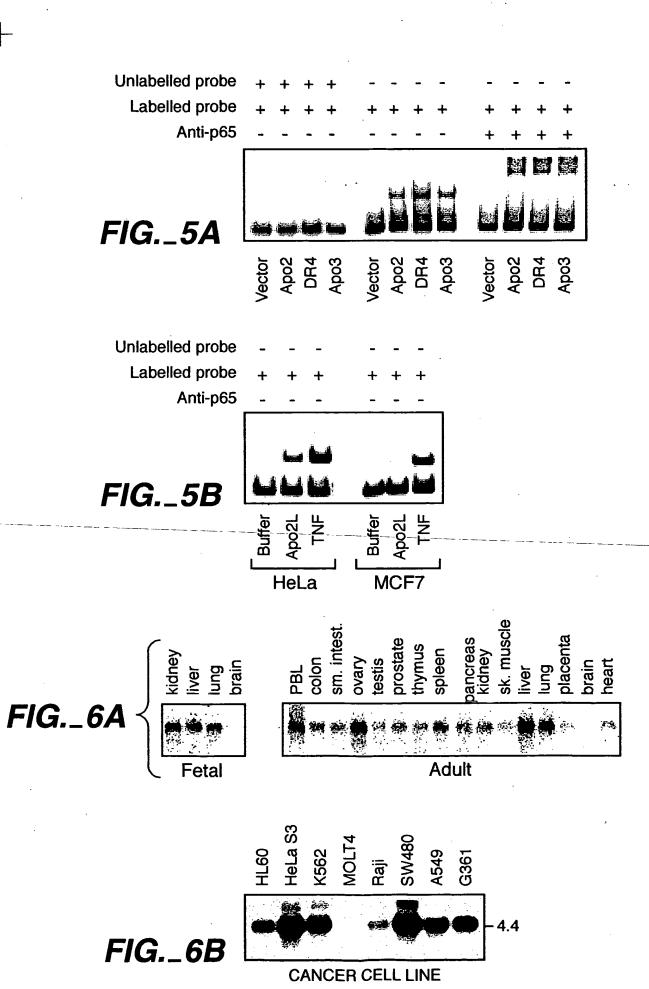


FIG.\_5C



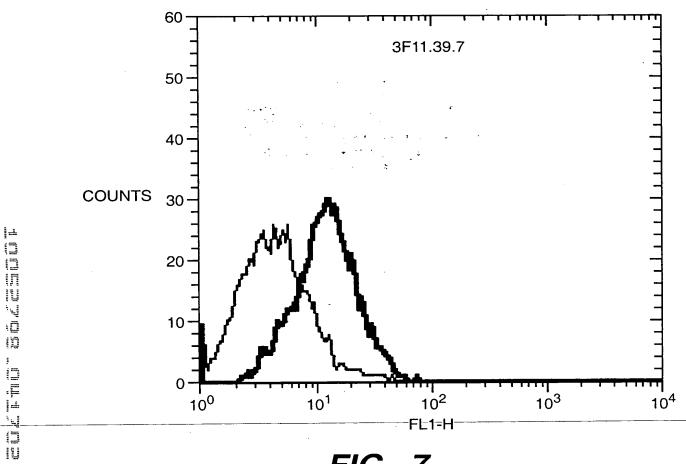
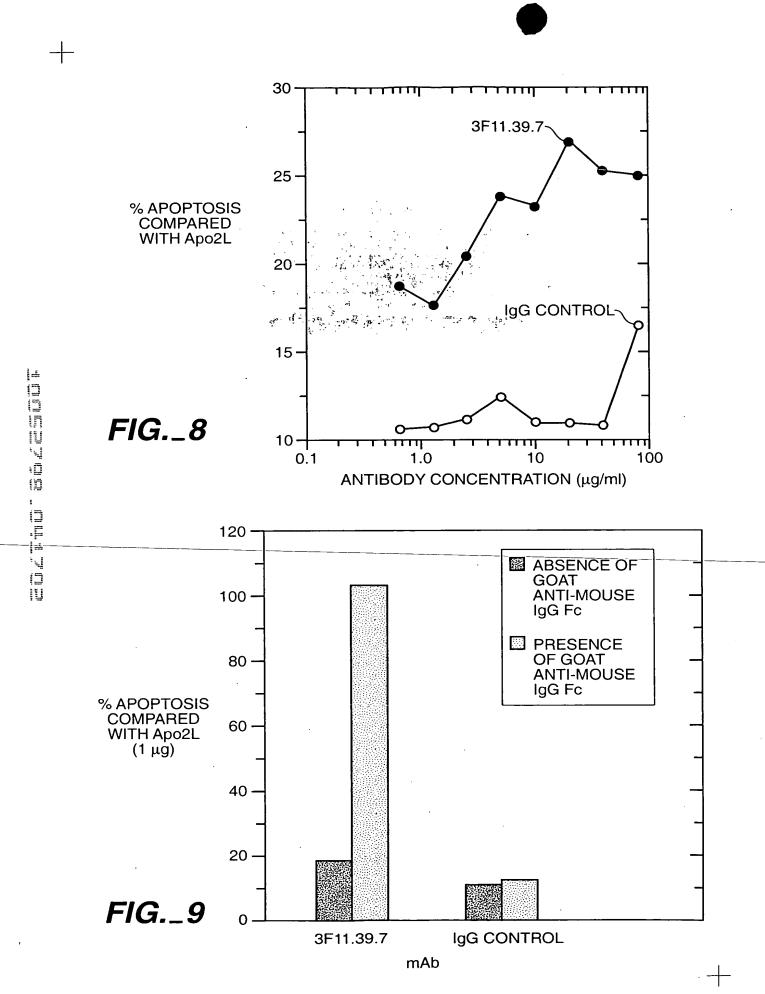
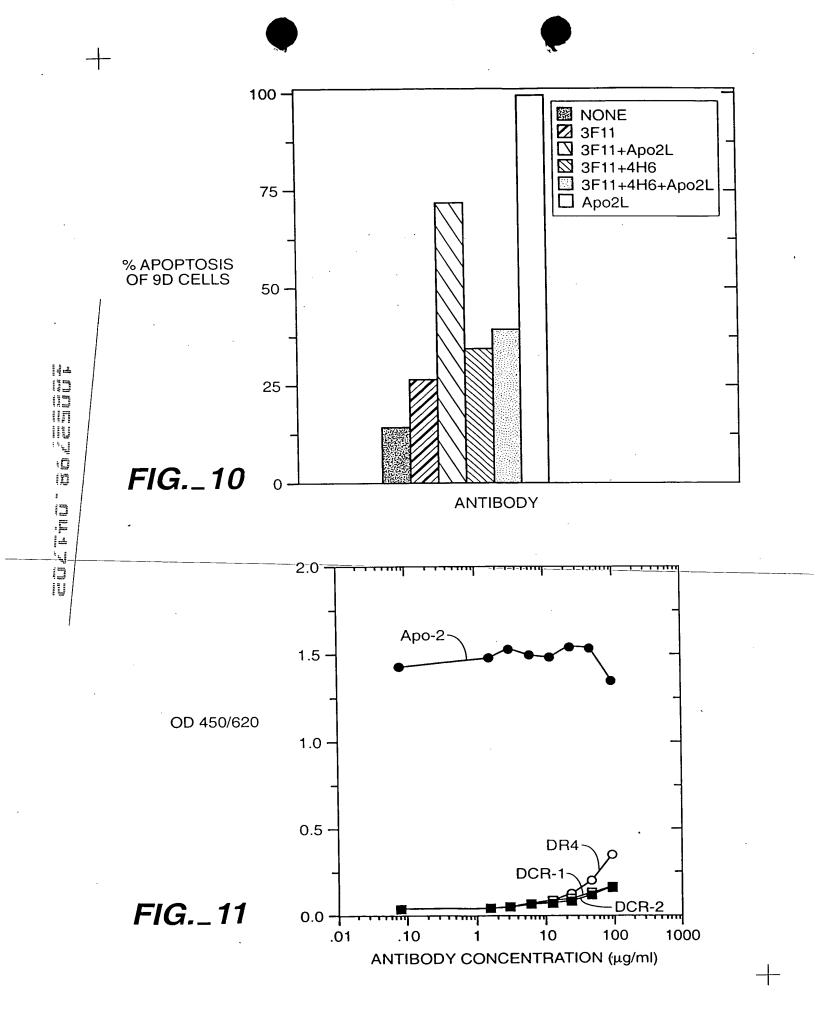


FIG.\_7





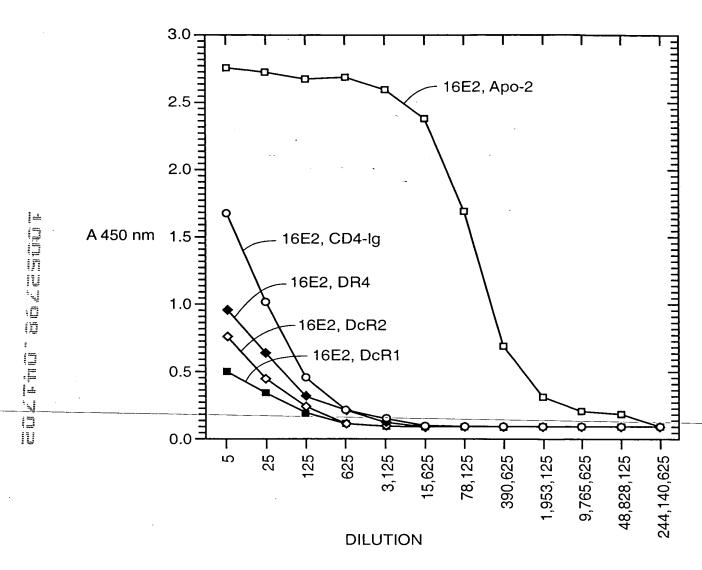


FIG.\_12A

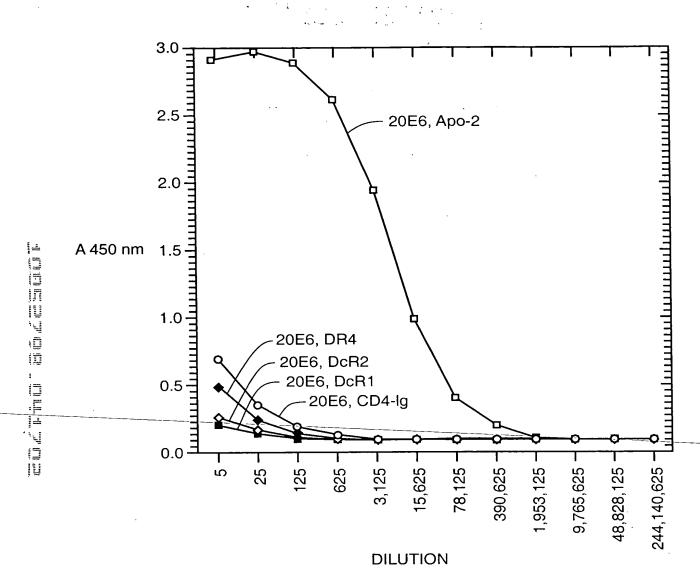


FIG.\_12B

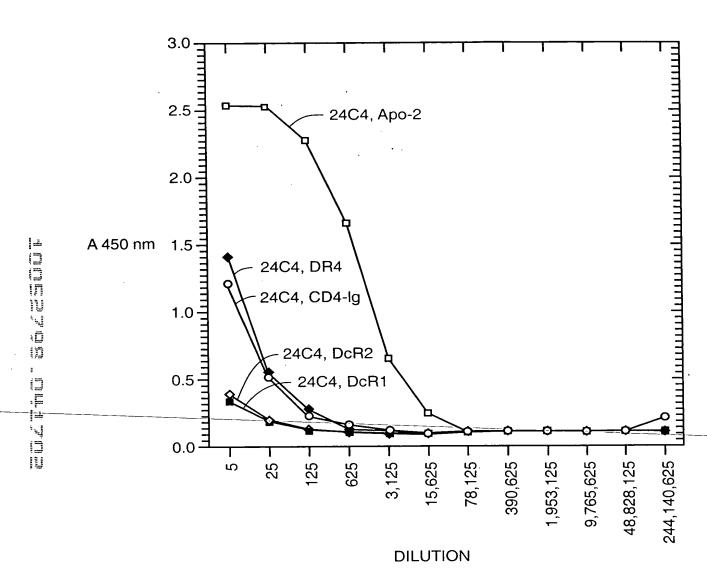
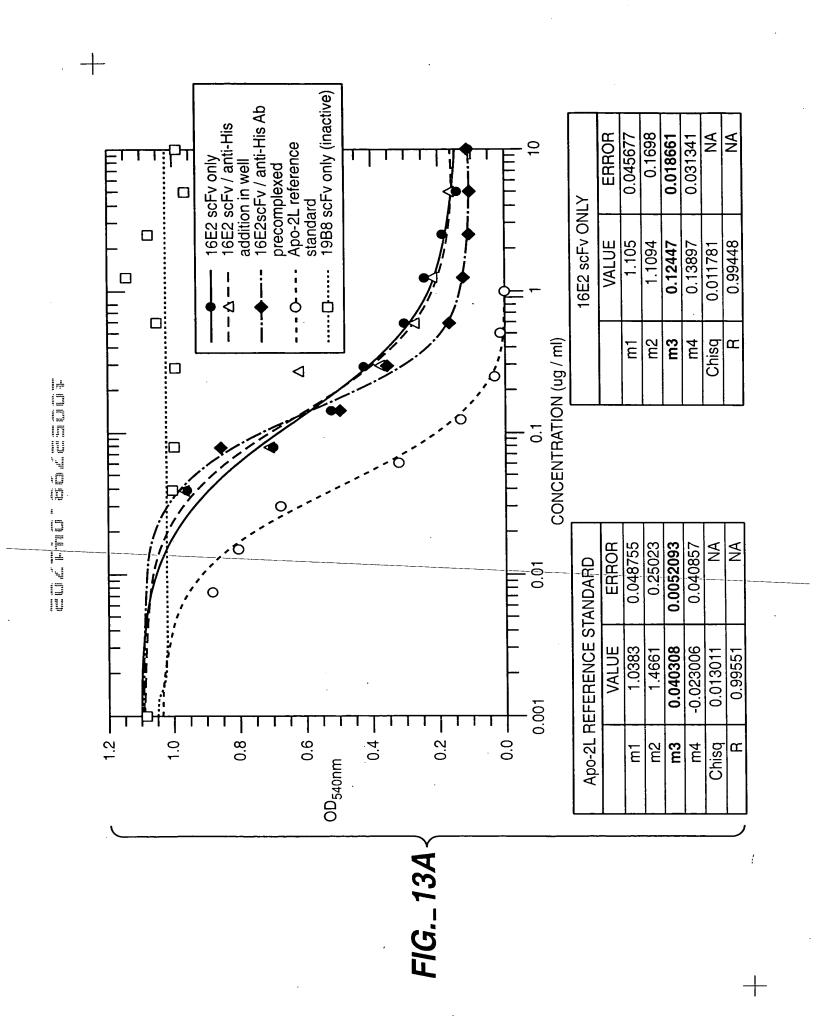
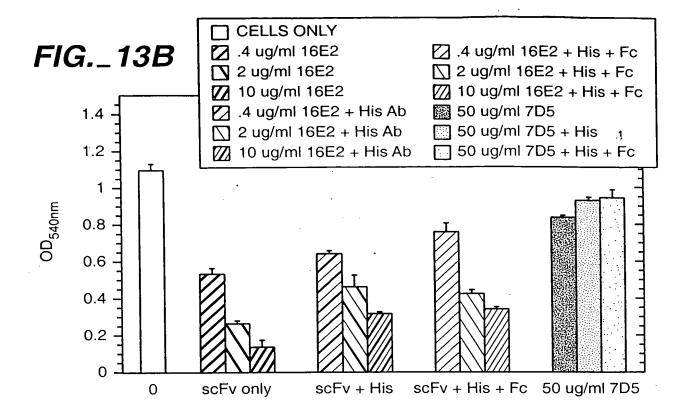
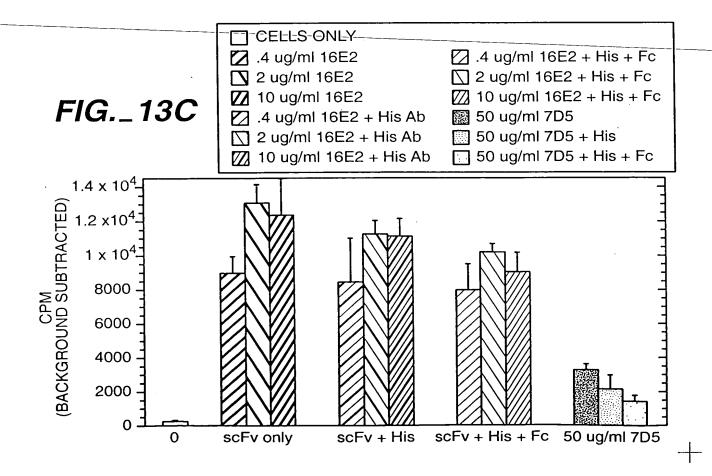


FIG.\_12C

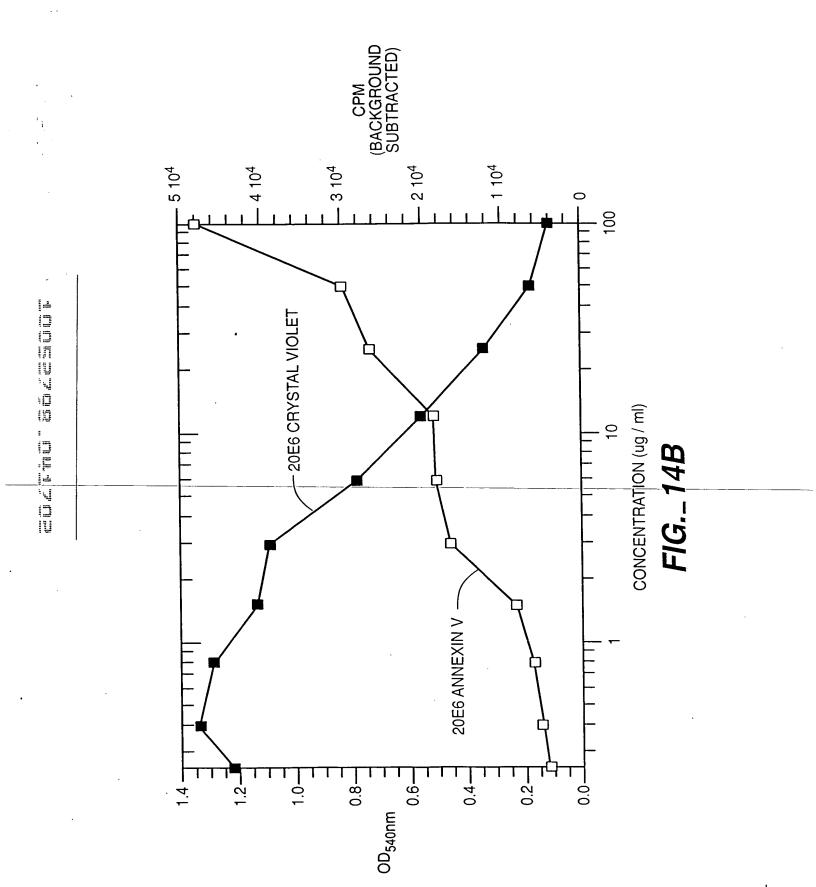
+

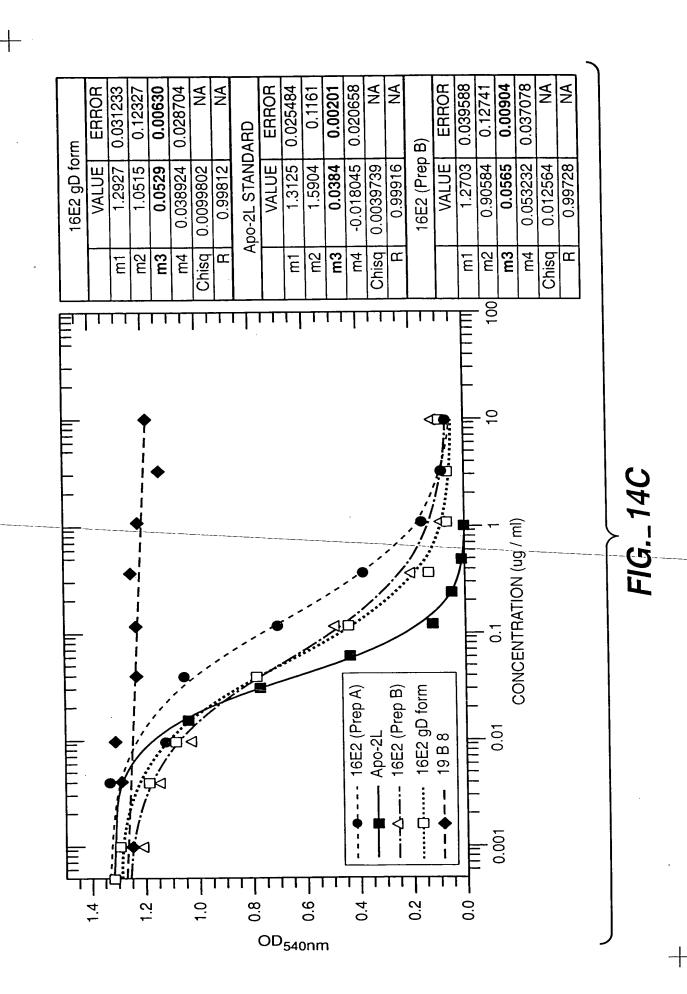












ATGACCATGA TTACGCCAAG CTTTGGAGCC TTTTTTTTGG AGATTTTCAA 50 CGTGAAAAA TTATTATTCG CAATTCCTTT AGTTGTTCCT TTCTATGCGG 100 CCCAGCCGGC CATGGCCGAG GTGCAGCTGG TGCAGTCTGG GGGAGGTGTG 150 GAACGGCCGG GGGGGTCCCT GAGACTCTCC TGTGCAGCCT CTGGATTCAC 200 CTTTGATGAT TATGGCATGA GCTGGGTCCG CCAAGCTCCA GGGAAGGGGC 250 TGGAGTGGGT CTCTGGTATT AATTGGAATG GTGGTAGCAC AGGATATGCA 300 GACTCTGTGA AGGGCCGAGT CACCATCTCC AGAGACAACG CCAAGAACTC 350 CCTGTATCTG CAAATGAACA GCCTGAGAGC CGAGGACACG GCCGTATATT 400 ACTGTGCGAA AATCCTGGGT GCCGGACGGG GCTGGTACTT CGATCTCTGG 450 GGGAAGGGGA CCACGGTCAC CGTCTCGAGT GGTGGAGGCG GTTCAGGCGG 500 AGGTGGCAGC GGCGGTGGCG GATCGTCTGA GCTGACTCAG GACCCTGCTG 550 TGTCTGTGGC CTTGGGACAG ACAGTCAGGA TCACATGCCA AGGAGACAGC 600 CTCAGAAGCT ATTATGCAAG CTGGTACCAG CAGAAGCCAG GACAGGCCCC 650 TGTACTTGTC ATCTATGGTA AAAACAACCG GCCCTCAGGG ATCCCAGACC 700 GATTCTCTGG CTCCAGCTCA GGAAACACAG CTTCCTTGAC CATCACTGGG 750 GCTCAGGCGG AAGATGAGGC TGACTATTAC TGTAACTCCC GGGACAGCAG 800 TGGTAACCAT GTGGTATTCG GCGGAGGGAC CAAGCTGACC GTCCTAGGTG 850 CGGCCGCACA TCATCATCAC CATCACGGGG CCGCAGAACA AAAACTCATC 900 TCAGAAGAGG ATCTGAATGG GGCCGCATAG 930

### FIG.\_15A

ATGACCATGA TTACGCCAAG CTTTGGAGCC TTTTTTTTGG AGATTTTCAA 50 CGTGAAAAA TTATTATTCG CAATTCCTTT AGTTGTTCCT TTCTATGCGG 100 CCCAGCCGGC CATGGCCGGG GTGCAGCTGG TGGAGTCTGG GGGAGGCTTG 150 GTCCAGCCTG GGGGGTCCCT GAGACTCTCC TGTGCAGCCT CTGGATTCAC 200 CTTTAGTAGC TATTGGATGA GCTGGGTCCG CCAGGCTCCA GGGAAGGGGC 250 TGGAGTGGGT GGCCAACATA AAGCAAGATG GAAGTGAGAA ATACTATGTG 300 GACTCTGTGA AGGGCCGATT CACCATCTCC AGAGACAACG CCAAGAACTC 350 ACTGTATCTG CAAATGAACA GCCTGAGAGC CGAGGACACG GCTGTGTATT 400 ACTGTGCGAG AGATCTTTTA AAGGTCAAGG GCAGCTCGTC TGGGTGGTTC 450 GACCCCTGGG GGAGAGGGAC CACGGTCACC GTCTCGAGTG GTGGAGGCGG 500 TTCAGGCGGA GGTGGTAGCG GCGGTGGCGG ATCGTCTGAG CTGACTCAGG 550 ACCCTGCTGT GTCTGTGGCC TTGGGACAGA CAGTCAGGAT CACATGCCAA 600 GGAGACAGCC TCAGAAGCTA TTATGCAAGC TGGTACCAGC AGAAGCCAGG 650 ACAGGCCCCT GTACTTGTCA TCTATGGTAA AAACAACCGG CCCTCAGGGA 700 TCCCAGACCG ATTCTCTGGC TCCAGCTCAG GAAACACAGC TTCCTTGACC 750 ATCACTGGGG CTCAGGCGGA AGATGAGGCT GACTATTACT GTAACTCCCG 800 GGACAGCAGT GGTAACCATG TGGTATTCGG CGGAGGGACC AAGCTGACCG 850 TCCTAGGTGC GGCCGCACAT CATCATCACC ATCACGGGGC CGCAGAACAA 900 AAACTCATCT CAGAAGAGGA TCTGAATGGG GCCGCATAG 939

FIG.\_15B

ATGACCATGA TTACGCCAAG CTTTGGAGCC TTTTTTTTGG AGATTTTCAA 50 CGTGAAAAA TTATTATTCG CAATTCCTTT AGTTGTTCCT TTCTATGCGG 100 CCCAGCCGGC CATGGCCCAG GTGCAGCTGG TGCAGTCTGG GGGAGGCGTG 150 GTCCAGCCTG GGCGGTCCCT GAGACTCTCC TGTGCAGCTT CTGGGTTCAT 200 TTTCAGTAGT TATGGGATGC ACTGGGTCCG CCAGGCTCCA GGCAAGGGGC 250 TGGAGTGGGT GGCAGGTATT TTTTATGATG GAGGTAATAA ATACTATGCA 300 GACTCCGTGA AGGGCCGATT CACCATCTCC AGAGACAATT CCAAGAACAC 350 GCTGTATCTG CAAATGAACA GCCTGAGAGC TGAGGACACG GCTGTGTATT 400 ACTGTGCGAG AGATAGGGGC TACTACTACA TGGACGTCTG GGGCAAAGGG 450 ACCACGGTCA CCGTCTCCTC AGGTGGAGGC GGTTCAGGCG GAGGTGGCTC 500 TGGCGGTGGC GGATCGCAGT CTGTGTTGAC GCAGCCGCCC TCAGTGTCTG 550 GGGCCCCAGG ACAGAGGGTC ACCATCTCCT GCACTGGGAG AAGCTCCAAC 600 ATCGGGGCAG GTCATGATGT ACACTGGTAC CAGCAACTTC CAGGAACAGC 650 CCCCAAACTC CTCATCTATG ATGACAGCAA TCGGCCCTCA GGGGTCCCTG 700 ACCGATTCTC TGGCTCCAGG TCTGGCACCT CAGCCTCCCT GGCCATCACT 750 GGGCTCCAGG CTGAAGATGA GGCTGATTAT TACTGCCAGT CCTATGACAG 800 CAGCCTGAGG GGTTCGGTAT TCGGCGGAGG GACCAAGGTC ACTGTCCTAG 850 GTGCGGCCGC ACATCATCAT CACCATCACG GGGCCGCAGA ACAAAAACTC 900 ATCTCAGAAG AGGATCTGAA TGGGGCCGCA TAG 933

## FIG.\_15C

# 

Heavy chain MTMITPSFGAFFLEIFNVKKLLFAIPLVVPFYAAQPAMAEVQLVQSGGGV MTMITPSFGAFFLEIFNVKKLLFAIPLVVPFYAAQPAMAGVQLVESGGGL MTMITPSFGAFFLEIFNVKKLLFAIPLVVPFYAAQPAMAQVQLVQSGGGV	CDR1 ERPGGSLRLSCAASGFTFD <u>DYGMS</u> WVRQAPGKGLEWVS <u>GINWNGGSTGYA</u> VQPGGSLRLSCAASGFTFS <u>SYWMS</u> WVRQAPGKGLEWVANIKQDGSEKYYV VQPGRSLRLSCAASGFIFS <u>SYGMH</u> WVRQAPGKGLEWVA <u>GIFYDGGNKYYV</u>	CDR3 <u>DSVKG</u> RVTI SRDNAKNSLYLQMNSLRAEDTAVYYCAK <u>ILGAGRGWY</u> <u>DSVKG</u> RFTI SRDNAKNSLYLQMNSLRAEDTAVYYCAR <u>DLLKVKGSSSGW-</u> <u>DSVKG</u> RFTI SRDNSKNTLYLQMNSLRAEDTAVYYCAR <u>DRGYY</u>	Light chain F-DLWGKGTTVTVSSGGGGSGGGGSGGGS-SELTQDPAVSVALGQTVRI F-DPWGRGTTVTVSSGGGGSGGGGGGGS-SELTQDPAVSVALGQTVRI YMDVWGKGTTVTVSSGGGGSGGGGGGGGSQSVLTQPPSVSGAPGQRVTI	CDR1  TCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGSSSG TCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGSSSG SCTGRSSNIGAGHDVHWYQQLPGTAPKLIYDDSNRPSGVPDRFSGSRSG	CDR3 NTASLTITGAQAEDEADYYC <u>NSRDSSGNHVV</u> FGGGTKLTVLGAAAHHHHH NTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGTKLTVLGAAAHHHHH TSASLAITGLQAEDEADYYCQ <u>SYDSSLRGSV</u> FGGGTKVTVLGAAAHHHH	HGAAEQKLISEEDLNGAA HGAAEQKLISEEDLNGAA HGAAEQKLISEEDLNGAA
signal MTMITPS MTMITPS	ERPGGSI VQPGGSI VQPGRSI	DSVKGRV DSVKGRF DSVKGRF	F-DLWGK F-DPWGR YMDVWGR	CDR1 TCQGDSI TCQGDSI SCTGRSS	NTASLTI NTASLTI TSASLAI	HGAAEQF HGAAEQF HGAAEQF
ਜਜਜ	51 51	101 101 101	147 150 143	195 198 193	242 245 243	292 295 293
Apo-2.16E2.his Apo-2.20E6.his Apo-2.24C4.his	Apo-2.16E2.his Apo-2.20E6.his Apo-2.24C4.his	Apo-2.16E2.his Apo-2.20E6.his Apo-2.24C4.his	Apo-2.16E2.his Apo-2.20E6.his Apo-2.24C4.his	Apo-2.16E2.his Apo-2.20E6.his Apo-2.24C4.his	Apo-2.16E2.his Apo-2.20E6.his Apo-2.24C4.his	Apo-2.16E2.his Apo-2.20E6.his Apo-2.24C4.his

FIG.\_16